REMARKS

Claim 1 has been amended. Now new matter has been added. Upon entry of this amendment, claims 1-40 are present and active in the application.

Request for Reconsideration

When imaging biological tissues, it is often desirable to enhance the signals measured from specific structures. Contrast agents, which produce a strong emission or reflection signal, have been utilized in virtually every imaging modality including ultrasound, computed tomography, magnetic resonance imaging, and optical microscopy.

Optical coherence tomography (OCT) is an emerging high-resolution medical and biological imaging technology. OCT is analogous to ultrasound B-mode imaging except reflections of low-coherence light are detected rather than sound. OCT detects changes in the backscattered amplitude and phase of light from structures in tissue. This imaging technique is attractive for medical imaging because it permits the imaging of tissue microstructure in situ, yielding micron-scale imaging resolution without the need for excision and histological processing. OCT can record structures such as cell membranes, nuclei, and other organelles based on morphology-dependent optical characteristics. Because OCT performs imaging using light, it has a one- to two-order-of-magnitude higher spatial resolution than ultrasound and does not require contact with tissue.

Despite the rapidly growing acceptance of OCT in biomedical imaging, there are presently few agents available for enhancing optical contrast. This is partly attributable to the use of NIR wavelengths (>800 nm) that are typically employed in OCT, which are outside the range of most optically active materials.

The present invention makes use of the discovery that *plasmon-resonant* nanoparticles can be used to enhance the contrast in analyses and imaging techniques that use electromagnetic radiation, particularly those techniques which use radiation in the frequency range of infrared to ultraviolet, such as optical coherence tomography, light microscopy, holography, confocal microscopy, polarization microscopy,

interference microscopy, multi-photon microscopy, and endoscopy. Moreover, metallic nanoparticles composed of gold, silver, and/or copper are particularly suited as contrast agents for OCT applications. Preferably, the nanoparticles are metallic *anisotropic* nanoparticles, which possess superior plasmon-resonant characteristics and may be fabricated in bimetallic forms to permit their use in OCT applications using switchable magnetic and electric fields. The nanoparticles efficiently absorb the incident optical radiation and can be used as hyperthermia agents, creating local thermal gradients that are sufficient to kill individual cells. These contrast agents can therefore be used simultaneously for the detection and imaging of targeted cells followed by hyperthermic ablation.

The rejection of claims 1-40 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 7,198,777 (Boppart et al.), is respectfully traversed. Boppart et al. discloses a method of forming an image by optical coherence tomography, including exposing a patient to electromagnetic radiation, collecting reflected electromagnetic radiation, and forming an image from the collected electromagnetic radiation, the improvement comprising administering a contrast agent to the patient to enhance contrast of the image. There is no mention at all within Boppart et al. of using *plasmon-resonant nanoparticles* as *optical contrast agents*, and furthermore, there is no reason found within Boppart et al. that would cause one to use plasmon-resonant nanoparticles as optical contrast agents. As a result, Applicants maintain that the claims of current application are patentably distinct from the claims found within Boppart et al.

The rejection of claims 1-21 under 35 U.S.C. § 103(a) as being unpatentable over Toublan et al. (NPL-"Magentically-inducible optical contrast agents for optical coherence tomography"), is respectfully traversed. Claim 1 of the present invention addresses the problem of forming an image of a sample comprising forming an image of a mixture, by exposing the mixture to electromagnetic radiation. The mixture comprises the sample and plasmon-resonant nanoparticles. The electromagnetic radiation is in the frequency range of infra-red to ultraviolet light, and as now claimed the *plasmon-resonant nanoparticles* are *anisotropic metallic nanoparticles*.

Toublan et al. is directed to contrast agents in medical and biological imaging to enhance the sensitivity of detection and improve the diagnostic ability of imaging techniques. Toublan et al. further discusses using microspheres of 0.5 to 5 microns in diameter with a 50 Å thick protein shell as optical contrast agents. The microspheres can be filled with scattering substances such as melanin or gold. Scattering substances such as melanin or gold are not necessarily *anisotropic* plasmon-resonant nanoparticles, since being an *anisotropic* plasmon-resonant nanoparticle depends on not only the size of the particle, but the particle's *shape* as well. (See Specification, Paragraphs [0031] and [0049]) Toublan et al. does not disclose that the size or shape of the microspheres conform to that of an *anisotropic plasmon-resonant* nanoparticle. Just because particles are of a certain material, i.e. gold, and can fit within a microsphere of a set size, i.e. between 0.5 to 5 microns in diameter, does not mean that the particles are *anisotropic plasmon resonant nanoparticles*.

The rejection of claims 22-40 under 35 U.S.C. § 103(a) as being unpatentable over Sokolov (US 2004/0023415) in view of Lee et al. (NPL-"Engineered Microsphere Contrast agents for Optical Coherence Tomography"), is respectfully traversed. Claim 22 of the present invention addresses the problem of forming an image by optical coherence tomography, including exposing a patient to electromagnetic radiation, collecting reflected electromagnetic radiation, and forming an image from the collected electromagnetic radiation. The improvement comprises administering *anisotropic metallic nanoparticles* to a patient to *enhance contrast* of the image, wherein the anisotropic metallic nanoparticles are *gold nanorods* with a *magnetic tip*.

Sokolov discloses methods and apparatuses for using biospecific contrast agents to enhance the imaging of cells. Even more particularly, it concerns using metal nanoparticles and quantum dots attached to probe molecules with a high affinity to a specific biomarker on the surface of pre-cancerous and cancerous cells to enhance the imaging of those cells. Sokolov also discloses that colloidal gold and silver nanoparticles exhibit beautiful and intense colors in the visible spectral region. (See Sokolov, paragraph [0071]). Sokolov then states that it is believed that these colors are the result of excitation of surface plasmon resonances in the metal particles and are extremely sensitive to particles' sizes, shapes, and aggregation state; dielectric

properties of the surrounding medium; adsorption of ions on the surface of the particles; etc. However, Sokolov does not teach or disclose administering *anisotropic* metallic nanoparticles to a patient. In fact, there is no mention whatsoever in Sokolov of using *anisotropic* metallic nanoparticles, and no reason is given as well. Furthermore, Sokolov fails to teach or disclose *anisotropic* metallic nanoparticles which are gold *nanorods* with a *magnetic tip*. There is no teaching or disclosure within Sokolov of using a nanorod at all, let alone a gold nonorod with a *magnetic tip,* since that would require a tip that is *not gold, and such a tip is not disclosed.* Furthermore, Lee et al. fails to cure all of the deficiencies of Sokolov. As a result, Applicants maintain that claims 22-40 are not anticipated by or obvious in view of the cited references, either alone or in combination.

CONCLUSION

Applicants submit that the application is now in condition for allowance. Early notice of such action is earnestly solicited.

Respectfully submitted,

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